

Search Plan and Results

Question

[What impact has mandatory folic acid fortification had on the incidence of colon cancer? \(DGAC 2010\)](#)

Date Searched

6/18/09

Inclusion Criteria

- *Subjects/population*: Human subjects
- *Age*: Children, men and women of all ages
- *Setting*: US and Canada and other countries with fortification policy
- *Health status*: Healthy and those with elevated chronic disease risk (coronary heart disease or cardiovascular disease, type 2 diabetes, metabolic syndrome and obesity)
- *Nutrition related problem/condition*: None.

Search Criteria

- *Study design preferences*: Randomized controlled trials or clinical controlled studies, large non-randomized observational studies, cohorts, case-control studies, systematic reviews and meta-analyses
- *Size of study groups*: The sample size must equal 10 adults for each study group. For example, this would include 10 patients in the intervention group and 10 patients in the control or comparison group
- *Study dropout rate*: Less than 20%; preference for smaller dropout rates
- *Year range*: June 2004 to June 2009
- *Authorship*: If an author is included on more than one review article or primary research article that is similar in content, the most recent review or article will be accepted and earlier versions will be rejected
- *Languages*: Limited to articles in English
- *Other*: Article must be published in peer-reviewed journal.

Exclusion Criteria

- *Subjects/population*: Populations outside of the US and Canada
- *Age*: Not applicable
- *Setting*: Hospitalized patients
- *Health status*: Medical treatment or therapy and diseased subjects (already diagnosed with disease related to study purpose)
- *Nutrition related problem/condition*: All conditions.

Search Criteria

- *Study design preferences:* Not applicable
- *Size of study groups:* Sample sizes less than 10
- *Study dropout rate:* If the dropout rate in a study is 20% or greater, the study will be rejected
- *Year range:* Prior to June 2004
- *Authorship:* Studies by same author similar in content
- *Languages:* Articles not in English
- *Other:* Abstracts or presentations and articles not peer reviewed (Web sites, magazine articles, Federal reports, etc.).

Search Terms: Search Vocabulary

Comparators

- Intake levels and consumption levels
- Fortification
- Supplementation.

Intermediate Biomarkers/Physiological Effects

Polyps.

Health Outcomes/Clinical Disease

Colon cancer.

Other Terms

NHANES.

Electronic Databases

("Folic Acid"[Mesh] OR "folate"[All Fields]) AND ("Food, Fortified"[Mesh] OR "Dietary Supplements"[Mesh] OR "diet"[MeSH Terms] OR intake[All Fields]) AND "english and humans"[Filter] AND ("Colorectal Neoplasms"[mesh] OR "polyps"[MeSH Terms])

Total hits from all electronic database searches: 570

Total articles identified to review from electronic databases: 31

Articles Identified Via Handsearch or Other Means

Summary of Articles Identified to Review

Number of Primary Articles Identified: 2

Number of Review Articles Identified: 0

Total Number of Articles Identified: 2

Number of Articles Reviewed but Excluded: 29

List of Articles Included for Evidence Analysis

Mason JB, Dickstein A, Jacques PF, Haggarty P, Selhub J, Dallal G, Rosenberg IH. [A temporal association between folic acid fortification and an increase in colorectal cancer rates may be illuminating important biological principles: A hypothesis.](#) *Cancer Epidemiol Biomarkers Prev.* 2007 Jul; 16(7): 1, 325-1, 329. PMID: 17626997.

Hirsch S, Sanchez H, Albala C, de la Maza MP, Barrera G, Leiva L, Bunout D. [Colon cancer in Chile before and after the start of the flour fortification program with folic acid.](#) *Eur J Gastroenterol Hepatol.* 2009 Apr; 21(4): 436-439. PMID: 19190501.

List of Excluded Articles with Reason

Article (A-K)	Reason for Exclusion
Ashktorab H, Begum R, Akhgar A, Smoot DT, Elbedawi M, Daremipouran M, Zhao A, Momen B, Giardiello FM. Folate status and risk of colorectal polyps in African Americans. www.ncbi.nlm.nih.gov/pubmed/17372834 <i>Dig Dis Sci.</i> 2007 Jun; 52(6): 1, 462-1, 470. Epub 2007 Mar 20. PMID: 17372834	Does not answer question. About gene-promoter.
Bird CL, Swendseid ME, Witte JS, Shikany JM, Hunt IF, Frankl HD, Lee ER, Longnecker MP, Haile RW. Red cell and plasma folate, folate consumption, and the risk of colorectal adenomatous polyps. <i>Cancer Epidemiol Biomarkers Prev.</i> 1995 Oct-Nov; 4(7): 709-714. PMID: 8672986	Article from 1995.
Bollheimer LC, Buettner R, Kullmann A, Kullmann F. Folate and its preventive potential in colorectal carcinogenesis. How strong is the biological and epidemiological evidence? <i>Crit Rev Oncol Hematol.</i> 2005 Jul; 55(1): 13-36. Review. PMID: 15927841	Not a systematic review.
Cole BF, Baron JA, Sandler RS, Haile RW, Ahnen DJ, Bresalier RS, McKeown-Eyssen G, Summers RW, Rothstein RI, Burke CA, Snover DC, Church TR, Allen JI, Robertson DJ, Beck GJ, Bond JH, Byers T, Mandel JS, Mott LA, Pearson LH, Barry EL, Rees JR, Marcon N, Saibil F, Ueland PM, Greenberg ER; Polyp Prevention Study Group. Folic acid for the prevention of colorectal adenomas: A randomized clinical trial. www.ncbi.nlm.nih.gov/pubmed/17551129 <i>JAMA.</i> 2007 Jun 6; 297(21): 2, 351-2, 359. PMID: 17551129	Does not answer question. About folic acid supplementation intervention.

Coogan PF, Rosenberg L. The use of folic acid antagonists and the risk of colorectal cancer . <i>Pharmacoepidemiol Drug Saf.</i> 2007 Oct; 16(10): 1, 111-1, 119. PMID: 17600846	Does not answer question. About folic acid antagonists.
Figueiredo JC, Levine AJ, Grau MV, Barry EL, Ueland PM, Ahnen DJ, Byers T, Bresalier RS, Summers RW, Bond J, McKeown-Eyssen GE, Sandler RS, Haile RW, Baron JA. Colorectal adenomas in a randomized folate trial: The role of baseline dietary and circulating folate levels. www.ncbi.nlm.nih.gov/pubmed/18843003 <i>Cancer Epidemiol Biomarkers Prev.</i> 2008 Oct; 17(10): 2, 625-2, 631. PMID: 18843003	Does not answer question. About folic acid supplementation intervention.
Flood A, Caprario L, Chatterjee N, Lacey JV Jr, Schairer C, Schatzkin A. Folate, methionine, alcohol, and colorectal cancer in a prospective study of women in the United States. <i>Cancer Causes Control.</i> 2002 Aug; 13(6): 551-561. PMID: 12195645	Does not answer question. About association between alcohol and folic acid consumption.
Fuchs CS, Willett WC, Colditz GA, Hunter DJ, Stampfer MJ, Speizer FE, Giovannucci EL. The influence of folate and multivitamin use on the familial risk of colon cancer in women. www.ncbi.nlm.nih.gov/pubmed/11895870 <i>Cancer Epidemiol Biomarkers Prev.</i> 2002 Mar; 11(3): 227-234. PMID: 11895870	Does not answer question. Evaluated association of folic acid with colon cancer risk.
Harnack L, Jacobs DR Jr, Nicodemus K, Lazovich D, Anderson K, Folsom AR. Relationship of folate, vitamin B-6, vitamin B-12, and methionine intake to incidence of colorectal cancers. www.ncbi.nlm.nih.gov/pubmed/12588695 <i>Nutr Cancer.</i> 2002; 43(2): 152-158. PMID: 12588695	Does not answer question. Assessed the relationship of folate, methionine and vitamins B ₆ and B ₁₂ to occurrence of cancers of the colon.
Jaszewski R, Misra S, Tobi M, Ullah N, Naumoff JA, Kucuk O, Levi E, Axelrod BN, Patel BB, Majumdar AP. Folic acid supplementation inhibits recurrence of colorectal adenomas: a randomized chemoprevention trial. www.ncbi.nlm.nih.gov/pubmed/18680228 <i>World J Gastroenterol.</i> 2008 Jul 28; 14(28): 4, 492-4, 498. PMID: 18680228	Does not answer question. About folic acid supplementation intervention. Measure recurrence of polyps.
Kato I, Dnistrian AM, Schwartz M, Toniolo P, Koenig K, Shore RE, Akhmedkhanov A, Zeleniuch-Jacquotte A, Riboli E. Serum folate, homocysteine and colorectal cancer risk in women: A nested case-control study. www.ncbi.nlm.nih.gov/pubmed/10206314 <i>Br J Cancer.</i> 1999 Apr; 79(11-12): 1, 917-1, 922. PMID: 10206314	Does not answer question. Assessed the relation of plasma folate and homocysteine and colorectal adenoma recurrence
Khosraviani K, Weir HP, Hamilton P, Moorehead J, Williamson K. Effect of folate supplementation on mucosal cell proliferation in high-risk patients for colon cancer. <i>Gut.</i> www.ncbi.nlm.nih.gov/pubmed/12117879 2002 Aug; 51(2): 195-199. PMID: 12117879	Lab study.
Kim YI, Baik HW, Fawaz K, Knox T, Lee YM, Norton R, Libby E, Mason JB. Effects of folate supplementation on two provisional molecular markers of colon cancer: A prospective, randomized trial. www.ncbi.nlm.nih.gov/pubmed/11197251 <i>Am J Gastroenterol.</i> 2001 Jan; 96(1): 184-195. PMID: 11197251	Does not answer question. Study of folate supplementation on genomic DNA methylation.
Kim YI. Folate and colorectal cancer: An evidence-based critical review . <i>Mol Nutr Food Res.</i> 2007 Mar; 51(3): 267-292. PMID: 17295418	Not a systematic review.
Kim YI. Role of folate in colon cancer development and progression . <i>J Nutr.</i> 2003 Nov; 133(11 Suppl 1): 3731S-3739S. Review. PMID: 14608107	Not a systematic review.
Konings EJ, Goldbohm RA, Brants HA, Saris WH, van den Brandt PA. Intake of dietary folate vitamers and risk of colorectal carcinoma: Results from The Netherlands Cohort Study. www.ncbi.nlm.nih.gov/pubmed/12237910 <i>Cancer.</i> 2002 Oct 1; 95(7): 1, 421-1, 433. PMID: 12237910	International.

Kune G, Watson L. Colorectal cancer protective effects and the dietary micronutrients folate, methionine, vitamins B6, B12, C, E, selenium, and lycopene. www.ncbi.nlm.nih.gov/pubmed/17176213 <i>Nutr Cancer</i> . 2006; 56(1): 11-21. PMID: 17176213	Does not answer question. International study (Australia) that assessed relationship of folate, methionine and vitamins B6 and B12 to occurrence of colon cancers.
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Article (L-R)	Reason for Exclusion
Luebeck EG, Moolgavkar SH, Liu AY, Boynton A, Ulrich CM. Does folic acid supplementation prevent or promote colorectal cancer? Results from model-based predictions. www.ncbi.nlm.nih.gov/pubmed/18539928 <i>Cancer Epidemiol Biomarkers Prev</i> . 2008 Jun; 17(6): 1, 360-1, 367. Epub 2008 Jun 6. PMID: 18539928	Does not answer question. Mathematical model.
Martínez ME, Giovannucci E, Jiang R, Henning SM, Jacobs ET, Thompson P, Smith-Warner SA, Alberts DS. Folate fortification, plasma folate, homocysteine and colorectal adenoma recurrence. http://www.ncbi.nlm.nih.gov/pubmed/16615116?ordinalpos=39&itool=Email_EmailReport_Pubmed_ReportSelector_Pubmed_RVDocSum <i>Int J Cancer</i> . 2006 Sep 15; 119(6): 1, 440-1, 446. PMID: 16615116	Does not answer question. Assessed the relation of plasma folate and homocysteine and colorectal adenoma recurrence.
Martínez ME, Henning SM, Alberts DS. Folate and colorectal neoplasia: Relation between plasma and dietary markers of folate and adenoma recurrence. www.ncbi.nlm.nih.gov/pubmed/15051616 <i>Am J Clin Nutr</i> . 2004 Apr; 79(4): 691-697. PMID: 15051616	Does not answer question. Assessed dietary markers of folate status and colorectal adenoma recurrence.
Murphy G, Sansbury LB, Cross AJ, Stolzenberg-Solomon R, Laiyemo A, Albert PS, Wang Z, Schatzkin A, Lehman T, Kalidindi A, Modali R, Lanza E. Folate and MTHFR: Risk of adenoma recurrence in the Polyp Prevention Trial. <i>Cancer Causes Control</i> . 2008 Sep; 19(7): 751-758. Epub 2008 Mar 6. PMID: 18322814	Does not answer question. About the association between MTHFR, total folate and the risk of colorectal adenoma recurrence.
Otani T, Iwasaki M, Sasazuki S, Inoue M, Tsugane S; Japan Public Health Center-based Prospective Study Group. Plasma folate and risk of colorectal cancer in a nested case-control study: the Japan Public Health Center-based prospective study. www.ncbi.nlm.nih.gov/pubmed/17943453 <i>Cancer Causes Control</i> . 2008 Feb; 19(1): 67-74. Epub 2007 Oct 18. PMID: 17943453	International.

Article (S-Z)	Reason for Exclusion
Sanjoaquin MA, Allen N, Couto E, Roddam AW, Key TJ. Folate intake and colorectal cancer risk: A meta-analytical approach. www.ncbi.nlm.nih.gov/pubmed/15499620 <i>Int J Cancer</i> . 2005 Feb 20; 113(5): 825-828. PMID: 15499620	Does not answer question. Examined the association between folate consumption and colorectal cancer risk.
Terry P, Jain M, Miller AB, Howe GR, Rohan TE. Dietary intake of folic acid and colorectal cancer risk in a cohort of women. www.ncbi.nlm.nih.gov/pubmed/11857369 <i>Int J Cancer</i> . 2002 Feb 20; 97(6): 864-867. PMID: 11857369	Does not answer question. Evaluated association between dietary folate intake and reduced colorectal cancer risk.
Sauer J, Mason JB, Choi SW. Too much folate: A risk factor for cancer and cardiovascular disease? <i>Curr Opin Clin Nutr Metab Care</i> . 2009 Jan; 12(1): 30-36. Review. PMID: 19057184	Does not answer question. Examined role of folate in chronic diseases, focusing on cancer and CVD.
Van Guelpen B, Hultdin J, Johansson I, Hallmans G, Stenling R, Riboli E, Winkvist A, Palmqvist R. Low folate levels may protect against colorectal cancer. www.ncbi.nlm.nih.gov/pubmed/16638790 <i>Gut</i> . 2006 Oct; 55(10): 1, 461-1, 466. Epub 2006 Apr 25. PMID: 16638790	International.

Zhang SM, Moore SC, Lin J, Cook NR, Manson JE, Lee IM, Buring JE. Folate, vitamin B6, multivitamin supplements, and colorectal cancer risk in women. www.ncbi.nlm.nih.gov/pubmed/16339055 *Am J Epidemiol.* 2006 Jan 15; 163(2): 108-115. Epub 2005 Dec 7. PMID: 16339055

Does not answer question. Evaluated associations between intakes of folate and vitamin B₆ and colorectal cancer risk among women enrolled in a randomized trial.